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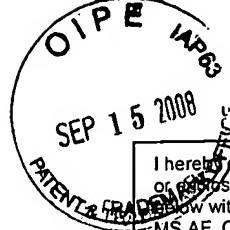
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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) CWRU-P03-003	
	Application Number 10/649,591	Filed August 26, 2003	
	First Named Inventor Sanford D. Markowitz		
	Art Unit 1643	Examiner S. L. Rawlings	
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <p><input type="checkbox"/> applicant /inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>54,144</u></p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____</p> <p> _____ Signature <u>Z. Angela Guo, Ph.D.</u> Typed or printed name <u>(617) 951-7546</u> Telephone number <u>September 11, 2008</u> Date</p> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			

<input checked="" type="checkbox"/> *Total of <u>1</u> forms are submitted.
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I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: MS AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
Dated: <u>9/11/08</u>	Signature: <u>Andrea Borden</u> (Andrea Borden)



I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to:  
MS AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: September 11, 2008

Signature

*Andrea Borden*  
(Andrea Borden)

Docket No.: CWRU-P03-003

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of: Markowitz, S. D.  
Application No.: 10/649,591  
Filed: August 26, 2003  
For: METHODS AND COMPOSITIONS FOR  
CATEGORIZING PATIENTS

Docket No.: CWRU-P03-003  
Confirmation No.: 4997  
Art Unit: 1643  
Examiner: Rawlings, S. L.

**REMARKS ACCOMPANYING PRE-APPEAL BRIEF REQUEST FOR REVIEW**

**MS AF**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Applicant respectfully requests a Pre-Appeal Brief Review. Request form PTO/SB/33 is filed herewith. Applicant respectfully requests reconsideration in view of the Response filed on March 31, 2008 as well as the following remarks.

**REMARKS**

Claim 75 and dependent claims 84-91, 93-102, 104-106, 123, and 124 remain rejected. Independent claim 75 recites a method for determining whether a subject is likely to have a colon neoplasm comprising obtaining a sample, and detecting at least one secreted ColoUp2 polypeptide selected from a polypeptide that is at least 95% identical to SEQ ID NO: 21 and a polypeptide that is at least 95% identical to SEQ ID NO: 3, wherein the presence of at least one secreted ColoUp2 polypeptide indicates that the subject is likely to have a colon neoplasm.

**Background**

Applicant notes that the rejections addressed below have previously been argued by Applicant, and subsequently withdrawn by the Examiner. Moreover, during a telephonic interview on March 16, 2007, the Examiner indicated that the claims limited to the method of detecting SEQ ID NO: 3 would be in condition for allowance. Furthermore, based on the Advisory Action mailed March 20, 2007, it appears that the Examiner would have allowed claims directed to a method for detecting an amino acid sequence that is at least 95% identical to SEQ ID NO: 3 (see Advisory Action, p. 2, lines 3-7, for example). However, contrary to what the Examiner had indicated (for example, in the Office Action dated July 6, 2006), the Examiner denied rejoinder of the non-elected subject matter (e.g., SEQ ID NO: 21). As such, Applicant declined the Examiner's proposed allowance of claims directed to SEQ ID NO: 3 and filed a Petition from restriction requirement on May 22, 2007 requesting rejoinder of SEQ ID NO: 21 and a polypeptide encoded by a polynucleotide having SEQ ID

NO: 5, with the elected SEQ ID NO: 3 for reasons detailed in the Petition. This request was subsequently granted for reasons stated in the Decision on Petition of June 26, 2007 and the Examiner was invited to review the Decision on Petition.

As the Decision indicates, SEQ ID NO: 21 is merely a *fragment* of SEQ ID NO: 3. Applicant also reminds the Examiner that claims 123 and 124 of the subject application are directed to, *inter alia*, a method of detecting a polypeptide having the sequence of SEQ ID NO: 21 or SEQ ID NO: 3, respectively. As such, it is unclear why the subject matter of at least claim 124 that was at one time deemed allowable by the Examiner, should remain rejected. As will be evident from the discussion below, following the decision of the request for a rejoinder, the Examiner has improperly reapplied a few rejections that were previously withdrawn.

35 U.S.C. §112, First Paragraph, Written Description

All claims remain rejected as allegedly lacking adequate written description. The Examiner maintains that "though the specification describes the polypeptides of SEQ ID NO: 3 and SEQ ID NO: 21 as members of the genus of secreted 'ColoUp2' polypeptides to which the claims are directed, neither polypeptide is reasonably deemed representative of the genus, as a whole, because there is no disclosure of a structural feature shared by each of [sic] member of the genus ... which correlates with any common functional feature attributable to the shared structural feature." Applicant respectfully disagrees.

As an initial matter, Applicant notes that claims 123 and 124 are directed to two specific sequences (SEQ ID NO: 3 or 21), rather than a genus. Accordingly, the current rejection clearly should not apply to those two claims. Applicant reiterates arguments made of record in the Responses dated November 6, 2006 and January 29, 2008. The specification provides ample description of the ColoUp2 polypeptides for the purposes of the claimed method, including the full-length secreted and processed forms of the ColoUp2 polypeptide and fragments thereof (see, e.g., p. 19, lines 14-24), as well as specific polymorphisms and various structural features as described at, e.g., p. 34, lines 4-18 (see also Response dated November 6, 2006, p. 15). Thus, contrary to the Examiner's assertion, the specification provides adequate structural features shared by the recited polypeptides. In addition, the Examiner retraces his prior conjecture regarding the alleged structural variability among the variants of SEQ ID NO: 3, asserting that "members of the claimed genus of polypeptides are expected to have functions that differ substantially from that of the disclosed mature, secreted polypeptide of SEQ ID NO: 3" (p. 8, lines 1-3 of Office Action dated March 11, 2008). The Examiner's reliance on the teachings of De Plaen et al. clearly lacks any logical basis with which to support his assertion. Applicant reiterates that the variability in structure and function among members of the *MAGE* genes is not surprising given their low percent identities to each other (e.g., as low as 57%). Indeed, these genes encode proteins that, although may have similar structural features, are different and distinct proteins under the control of different regulatory sequences (see, e.g., abstract). In contrast, claim 75 recites a polypeptide that is at least 95%

identical to SEQ ID NOs: 3 or 21 and, therefore, excludes polypeptides that are, for example, 60% identical to SEQ ID NO: 3 but that may be in the same family as ColoUp2.

Applicant notes that in the Office Action dated September 17, 2007, the Examiner asserted: "if not a polypeptide comprising the amino acid sequences of SEQ ID NO: 3 and/or SEQ ID NO: 21, the specification fails to describe with any of the requisite degree of clarity and particularity the structures of the secreted 'ColoUp2' polypeptides that [are] encoded by a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 5" (see p. 10, third paragraph). Accordingly, solely to expedite prosecution, Applicant amended claim 75 to remove the reference to the nucleotide sequence of SEQ ID NO: 5 and to instead specify the ColoUp2 polypeptide by reference to "at least 95% identical to" SEQ ID NO: 3 or 21. However, the Examiner appears to require a further limitation on the ColoUp2 polypeptide sequences. As argued above, the specification clearly provides adequate written description for the scope of polypeptides claimed, as also previously acknowledged by the Examiner. Applicant respectfully requests that this rejection be withdrawn.

35 U.S.C. §112, First Paragraph, Enablement

All claims remain rejected for alleged lack of enablement. Similar to the written description rejection, the Examiner alleges that since the variants of SEQ ID NOs: 3 and 21 differ structurally and functionally, a skilled artisan cannot predict which of such variants could serve as biomarkers of the disease. The Examiner continues to assert that the specification fails to demonstrate the presence of any of the claimed polypeptides in any biological sample.

As noted above, claims 123 and 124 are directed to two specific sequences (SEQ ID NO: 3 or 21), rather than a genus, and the current rejection should not apply to those two claims. Applicant has clearly described in previous Responses that the application does indeed demonstrate the presence of such polypeptides and even pointed to discrete passages in the specification where such support can be found. However, it appears that the Examiner has taken on a new position, demanding examples from *human* subjects (see Office Action dated March 11, 2008, p. 19, lines 5-8). Applicants wish to point out that the scope of enablement only needs to bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); MPEP 2164.08. There is no requirement in U.S. patent law that the claimed invention must work 100% of the time under all conceivable circumstances. "All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art." MPEP 2164.08. Applicants submit that the data presented in the specification more than satisfy the "reasonable correlation" of the in vitro or in vivo working examples with the claimed method as required by case law.

The Examiner continues to allege that because the polypeptides of the genus have vastly differing structures and functions, it is *expected* that the presence in a biological sample of *most* of the polypeptides

would *not* provide an indication of the presence of such a disease (Office Action of March 11, 2008, p. 19, 4<sup>th</sup> full paragraph). The Examiner appears certain in his proposition and seems to require demonstration of the functionality of every claimed species. However, Applicant reminds the Examiner that there is no legal requirement to test the efficacy of all biological samples of the claimed invention to prove operativeness. The law does not impose such a formidable burden on inventors seeking patent protection and should not be held to such unreasonable standards. "Appellants (here, Applicant) are not required to disclose every species encompassed by their claims even in an unpredictable art" (emphasis in original). *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976). As outlined in previous Responses, Applicant has clearly demonstrated the presence of a secreted ColoUp2 polypeptide in a biological sample as well as methods of detecting such polypeptides secreted from an animal in an established model system. Accordingly, the pending claims are fully enabled throughout their scope. Applicant respectfully requests that this rejection be withdrawn.

#### Priority

The Examiner maintains that none of the claims can properly receive benefit under 35 U.S.C. §120 by the earlier filing dates of the priority documents cited because all claims stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description and a sufficiently enabling disclosure. As such, the effective filing date of all claims is deemed the filing date of the instant application, namely August 26, 2003. Applicant respectfully disagrees for the reasons already made of record.

The present application amply describes and more than adequately enables the full scope of the pending claims. Applicant notes that this assertion was previously withdrawn in the Office Action dated December 19, 2006 (see p. 2, section 6). Except for claims 86, 87, 98, and 99, the Examiner indicated that all other claims properly benefit under 35 U.S.C. §120 by the filing date of the earlier filed U.S. Patent Application No. 10/229,345, namely August 26, 2002. Applicant reiterates that the pending claims do not differ in scope as compared to previously allowable subject matter to warrant a new rejection under §112. Thus, the effective filing date of the pending claims should be the filing date of the earliest priority application, namely August 26, 2002.

#### 35 U.S.C. §102

A. Claims 75, 84-87, 89-91, 93-98, 100-102, 104-106, 123, and 124 stand rejected under USC 102(e) as allegedly being anticipated by US 2004/0005563 A1, Mack et al. (herein "Mack"). Applicant maintains that Mack does not teach or suggest a method for determining whether a subject is likely to have a colon neoplasm based on the presence of a secreted ColoUp2 polypeptide. Mack is entirely silent with respect to colon neoplasm; rather, this application is directed to ovarian cancer. Therefore, Mack clearly does not meet the standard for anticipating a claim as set forth in MPEP 2131. Yet, the Examiner persists: "though Applicant

intends the process is used to determine whether a subject is likely to have a colon neoplasm, the active process taught by the prior art is materially and manipulatively indistinguishable from that of the claimed process" (Office Action dated March 11, 2008, p. 28, lines 3-6). However, the Examiner fails to acknowledge that the recitation "colon neoplasm" constitutes a structural element of claim 75 since it is recited in both the preamble and the "wherein" clause. Accordingly, Mack fails to teach all the elements of independent claim 75 and all the claims that depend therefrom.


B. Claims 75, 84-87, 89-91, 93-98, 100-102, and 104-106 remain rejected under USC 102(a) as allegedly being anticipated by WO 2002/068677 A1, Mack et al. (herein '677), published September 6, 2002. The Examiner previously acknowledged the priority benefit of all claims to be the filing date of the earliest priority application, i.e., August 26, 2002, and consequently withdrew this rejection (Office Action dated December 19, 2006, p. 4, section 7). The Examiner's reason for reapplying this reference as 102(a) prior art has been noted above. However, Applicant reiterates that the pending claims do not differ in scope as compared to previously allowable subject matter to warrant a new rejection under §112. Accordingly, the Examiner has improperly reapplied this reference for at least the reason that it does not qualify as prior art under 102(a). The Office is invited to review prior arguments submitted in, e.g., the Response dated January 29, 2008, pp. 16-18. Applicant respectfully requests that this rejection be withdrawn.

C. Claims 75, 84-87, 89-91, 93-102, 104-106, 123 and 124 remain rejected under USC 102(a) as allegedly being anticipated by WO 2002/86443 A2, Aziz et al. (herein "Aziz"), published October 31, 2002. Similar to the '677 application above, Aziz fails to qualify as prior art under 102(a). The Office is invited to review prior arguments submitted in, e.g., the Response dated January 29, 2008, pp. 18-19. Applicant respectfully requests that this rejection be withdrawn.

For the reasons presented above, Applicants respectfully request that the foregoing rejections be withdrawn. If there are any other fees due, please charge our **Deposit Account No. 18-1945**, under Order No. **CWRU-P03-003** from which the undersigned is authorized to draw.

Dated: September 11, 2008

Respectfully submitted,

By   
Z. Angela Guo

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